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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,970	MARKHAM ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7,9,11,12,14 and 25-46* is/are pending in the application.

4a) Of the above claim(s) *9,11,12,14,25-27 and 31-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7 and 28-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/17/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 28 March 2002 as the U.S. national stage of international application PCT/GB00/00537 filed 18 February 2000, which claims benefit of UK application 9903694.9 filed 19 February 1999. The preliminary amendment filed 28 March 2002 has been entered. Claims 1-24 were originally filed. Claims 5, 6, 8, 10, 13, and 15-24 were canceled, claims 1-4, 7, 9, 11, 12 and 14 were amended and claims 25-46 were added in the 28 March Amendment. Claims 1-4, 7, 9, 11, 12, 14 and 25-46 are pending.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-4, 7 and 28-30) in the Paper filed 19 April 2004 is acknowledged. The traversal is on the ground(s) that examination of the claims of Groups I-IX concurrently would not present an undue burden. This is not found persuasive because the present application is filed under 35 U.S.C. §371 and therefore subject to restriction according to PCT Rule 13. As burden is not a factor to be considered in determining unity of invention, Applicant's argument is not germane to the present case.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 11, 12, 14, 25-27 and 31-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claims 1-4, 7 and 28-30 are presently under consideration.

It is noted that the examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found

allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 7 and 28-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The instant claims are directed to a nucleic acid encoding a latency promoter comprising a nucleic acid sequence which has at least 75% homology with the sequence set forth as SEQ IDNO: 1. On page 8, the specification states, "DNAs of the present invention include those of closely related sequences to, and having essentially the same biological properties as, the promoter disclosed herein, and particularly the DNA disclosed herein as SEQ ID NO: 1. This definition is intended to encompass natural allelic variations therein." Thus, the claims are

generic to any nucleic acid having at least 75% homology to SEQ ID NO: 1 and "essentially the same biological properties as the disclosed latency promoter". Further, according to the definition provided in the specification, the claims are explicitly directed naturally occurring allelic variants of the disclosed nucleic acid.

The Guidelines for Written Description state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (MPEP §2163(3)(a)(ii)).

The instant specification discloses four fragments of the HVS ORF73 promoter having the function of a latency promoter. The fragments comprise 630, 1000, 1500 and 2000 base pairs immediately upstream of the initiation codon of ORF 73 (see especially the first full paragraph on page 17). The 2000 base pair fragment is presumably SEQ ID NO: 1. However, these fragments are far from representative of the large and structurally divergent genus encompassed by the claims. The specification fails to set forth the relevant structural characteristics of the claimed nucleic acid such that the skilled artisan could distinguish those nucleic acids having the function of a latency promoter from those nucleic acids that do not have that function. Thus, outside of a nucleic acid comprising at least 630 base pairs immediately upstream of the

initiation codon of ORF 73 as set forth in SEQ ID NO: 1, the specification fails to convey the relevant, identifying characteristics of the claimed invention sufficient to show possession of the genus.

With regard to naturally occurring allelic variants, the specification provides no description of how the structure of the disclosed nucleic acid relates to the structure of any strictly neutral alleles. The general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others. As the common attributes of the subgenus of naturally occurring allelic variants are not described, one of skill in the art would conclude that applicant was not in possession of the full scope of the invention.

Finally, although the specification describes a method by which nucleic acids having the function of a latency promoter might be identified, an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property (*i.e.,* it has essentially the same biological properties as a latency promoter comprising SEQ ID NO: 1) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before

it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of any nucleic acid nucleic acid having at least 75% homology to SEQ ID NO: 1 and "essentially the same biological properties as the disclosed latency promoter", or any naturally occurring allelic variant of the disclosed nucleic acid. Therefore, only the described nucleic acid comprising at least 630 base pairs of sequence immediately upstream of the initiation codon of ORF73 as set forth in SEQ ID NO: 1 meet the written description provision of 35 U.S.C. §112, first paragraph.

Claims 1-3, 4, 7 and 28-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a latency promoter comprising at least 630 base pairs of sequence immediately upstream of the initiation codon of ORF73 as set forth in SEQ ID NO: 1, does not reasonably provide enablement for the broad scope of any nucleic acid encoding a latency promoter and which has at least 75% homology with SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and

whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claims are generic to any nucleic acid having at least 75% homology to SEQ ID NO: 1 and essentially the same biological properties as the disclosed latency promoter (*Id.*), which nucleic acid has utility for expressing proteins.

State of the prior art and level of predictability in the art: The art teaches that the functional determinants of any given promoter molecule are complex, and that the effect of modifying any given nucleic acid in a promoter sequence is not readily predicted. For example, according to the teachings of Arnone *et al.* (1997) *Development* 124:1851-1864, the claimed nucleic acid might be considered a regulatory module. Arnone *et al.* teaches that individual regulatory modules are always found to contain multiple transcription factor target sites, and these contribute in various ways to the overall regulatory output (paragraph bridging pages 1851-1852). Arnone *et al.* further teaches that an underestimate of the number of diverse transcription factor interactions found within regulatory modules is approximately 6.2 (first full paragraph on page 1853). Still further, Arnone *et al.* teaches, "[t]here are no examples of regulatory modules serviced only by homeodomain proteins, or Zn finger proteins, and so forth. This suggests diversity in the nature of the protein:protein interactions that are required of the factors in order

for each module to generate and communicate its regulatory output" (second full paragraph on page 1853). Thus, Arnone *et al.* teaches that promoters are comprised of a variety of regulatory elements which work in concert to provide the functional characteristics of any given promoter.

With regard to the particular structural features that confer the functional characteristics of a latency promoter, the art is silent. Thus, the skilled artisan is dependent upon the teachings of the specification to provide the manner and process of making the full scope of any nucleic acid having at least 75% homology to SEQ ID NO: 1 and essentially the same biological properties as the disclosed latency promoter in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention without undue experimentation.

Amount of direction provided by the inventor and existence of working examples: The instant specification discloses four fragments of the HVS ORF73 promoter having the function of a latency promoter (*Id.*). Although fragments comprising 630, 1000, 1500 and 2000 base pairs immediately upstream of the initiation codon of ORF 73 are indicated to retain the function of a latency promoter (see especially the first full paragraph on page 17), the specification does not identify the regulatory elements required for this function beyond that they lie within 630 base pairs of the ORF 73 initiation codon.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, making the full scope of the claimed invention would require undue experimentation. The claims are directed to a genus of nucleic acids having certain structural and functional limitations. However, neither the relevant art nor the instant disclosure identifies the structural elements required to provide the recited

function. Thus, the skilled artisan would not be able to distinguish the operative embodiments of the claimed invention from those that are inoperative without having to resort to empirical experimentation. Although the presence of inoperative embodiments within the scope of the claim does not necessarily render a claim non-enabled (see *Atlas Powder Co. v. E.I. du Pont de Nemours & Co* (224 USPQ 409, 414). *Atlas* also provides, "[o]f course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the claimed invention, the claims might indeed be invalid" (page 414). In the instant case, the structural limitations recited in the claims encompass many thousands of possible combinations, and many, if not most of these combinations would be inoperative. As identifying the operative embodiments within the scope of the claims would require a large amount of empirical experimentation, the amount of experimentation required to make the full scope of the claimed invention would clearly be undue. Therefore, the disclosure fails to enable the full scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 28 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to a nucleic acid having at least 75% homology to SEQ ID NO: 1 and capable of hybridizing under stringent conditions to the sequence set forth in SEQ ID NO: 1 and having essentially the same biological properties as the disclosed latency promoter. Given

that the art recognizes that nucleic acid molecules hybridize to complementary sequences, one of ordinary skill would not expect a nucleic acid comprising SEQ ID NO: 1 to hybridize to another nucleic acid molecule comprising SEQ ID NO: 1. Although it is possible that a nucleic acid within the scope of having 75% homology to SEQ ID NO: 1 might possess sufficient complementarity to hybridize under the conditions set forth in the claim, it would seem unlikely that Applicant's intention is to claim such an odd molecule. It would seem more likely that Applicant intends to capture molecules that are complementary to SEQ ID NO: 1; in which case, reciting that the nucleic acid is homologous to SEQ ID NO: 1 is improper. Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 4, 7 and 28-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicholas *et al.* (1992) *Virol.* 188:296-310 as evidenced by Entrez Nucleotide Database Accession No. M86409.

Nicholas *et al.* discloses a composition comprising isolated nucleic acid fragments of the HVS L-DNA in plasmid vectors (see especially the sections entitled "Recombinant plasmids" and "M13 subcloning and DNA sequencing" on page 297). Sequence obtained from this nucleic acid composition is disclosed as Accession No. M86409, which is 100% complementary to the

instant SEQ ID NO: 1 and demonstrates that the composition, which comprises double stranded DNA, also comprises the nucleic acid set forth in the instant application as SEQ ID NO: 1. Thus, the nucleic acid of Nicholas *et al.* anticipates the nucleic acid of claims 1 and 2, and the recombinant DNA molecule of claims 7 and 28.

Claims 3, 4, 29 and 30 further limit the latency promoter of the nucleic acid to being encoded by a nucleic acid sequence of a certain specified length. This limitation is inherent to the nucleic acid of Nicholas *et al.* because the promoter sequence disclosed thereby is the same as the promoter sequence claimed. Although the nucleic acid in which the promoter sequence is comprised is longer than 2000 base pairs, the portion of that DNA encoding the promoter itself would be constant unless one were to insert sequence into or delete sequence from the portion of the molecule that actually encodes the promoter. Therefore, the nucleic acid and recombinant DNA of Nicholas *et al.* also anticipates claims 3, 4, 29 and 30.

Nicholas *et al.* teaches a nucleic acid and recombinant DNA having all of the limitations of the instant claims; therefore, the claims are anticipated by Nicholas *et al.*

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DMS

Anne-Marie Falk

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